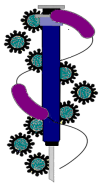
Technologies appropriate for short, middle, and long term goals

Regulatory Processes

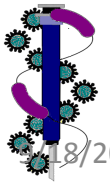


The Myth

- Hepatitis B is too complex a vaccine for developing country manufacturers. They cannot master recombinant technology
- Hib is too complex for developing country manufacturers. They cannot master conjugation
- In fact there are multiple DC manufacturers that have mastered these technologies. The pressing need is for national regulatory structures to come up to speed

National Regulatory Functions

- A regulatory system well defined by enabling legislation
- Ability to provide valid marketing authorization
- Capacity to authorize and oversee clinical trials
- Functional mechanism for monitoring, investigating and resolving adverse events
- Laboratory capacity to validate and perform necessary tests
- Rigorous lot release system
- Power to enforce Good Practices and quality systems in manufacturing facilities



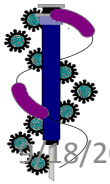
Prequalification: a barrier and a bridge

- Provides manufacturers an entree to sell on United Nations market
- Indicates achievement to « Gold Standard » level to sell outside the country
- Often required for domestic sales as well

Therefore the first priority is to assure that all manufacturers have access to the needed regulatory oversight for prequalification

Major shortcomings in regulatory systems for current developing country manufacturers

- Ability to:
  - Analyze complex registration file involving complex production technologies
  - Appropriately test product samples
  - Oversee and enforce manufacturer quality systems
  - Authorize and oversee clinical trials
  - Predict and expeditiously monitor and investigate potential safety risks
  - Pick up quality system defects through review of lot summary protocols



Proposed options

- Working through exisiting regulatory capacity building organizations
- Twinning of regulatory authorities
- Joint workshops with manufacturer groups
- Workshops in specific technologies

Examples of technologies

Technologies to encourage

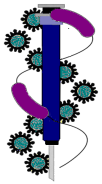
- Cell free systems
- Well-characterized products
- Involving standardizeable predictive tests
- Yielding correlates of protection

Technologies with potential problems

- Based on eggs or animal substrates
- Involving partially purified organisms
- Requiring animal tests
- Lack of insight into mechanisms of protection

Constraints

- Human resources
  - Highly capable regulatory experts
  - Government employees not well paid
- Capacity building
  - WHO activities, funds limited
  - NRA twinning
  - Regional or specialized networks, AVAREF, DCVRN
- Facilities and equipment
  - Clinical trial oversight, GMP enforcement require funds
  - Lab expertise expensive for testing and test development



Conclusions

- In terms of optimal regulation, there are priority areas for training of NRAs and NCLs, and proven ways to do that
- To enhance the ability of less experienced regulatory agencies to oversee marketing authorization and use of new vaccines, there are technologies that may be prioritized